

**REMARKS**

By the foregoing Amendment Applicant has combined the limitations of the previous Claim 5 with independent Claim 1 and cancelled Claim 5; combined the previous limitations of dependent Claim 10 with independent Claim 6 and cancelled Claim 10; and combined limitations of the previous Claim 15 with independent Claim 11 and cancelled Claim 15. Accordingly, as each of Claims 5, 10 and 15 have been previously examined their combination with the independent claims does not raise new issues nor the issue of new matter as they have already been subject to examination and rejection by the Examiner based upon prior art.

Reconsideration of the previous rejections under 35 U.S.C. 103(a) is respectfully requested in view of the following comments.

Although the Examiner has stated that he has considered the examples in the Specification, it appears that he has not considered, nor fully appreciated, the unexpected effect of the invention as set forth in such examples.

The present invention can exhibit the unexpected effect that by transvaginally administering 1, 25-dihydroxyvitamin D<sub>3</sub> to domestic animals, 1, 25-dihydroxyvitamin D<sub>3</sub> is "dose-dependently" absorbed, which effect cannot be expected in the case of peroral administration.

Moreover, since bioavailability of 1, 25-dihydroxyvitamin D<sub>3</sub> is much higher and absorption proceeds faster than in case of transvaginal administration than in the case of peroral or intraperitoneal administration, the present invention can be used for treatment of hypocalcemia of domestic animals. See the present Specification of pages 20-22. This effect could not have been taught, suggested or obviousness even with the proposed combination of cited references.

As the Examiner concedes, the primary references do not teach transvaginal administration and with respect to the Tjondronwgoro reference, such only describes transvaginal administration of progesterone to control bovine estrus in the specification at pages 2, lines 1-5. None of the cited references, including the Tjondronwgoro reference describes or suggest any problems in methods of administering vitamin D for treatment of hypocalcemia and the unexpected effect obtained by transvaginally administering "1, 25-dihydroxyvitamin D<sub>3</sub>" is clearly not disclosed.

In view of the foregoing Applicants respectfully submit that the proposed combination of references does not establish a *prima facie* case of obviousness for the invention, nor would such references, even in light of the ordinary skill possessed by the worker in the art, make obvious to the claimed invention. For the foregoing reasons, Applicants respectfully submit that the claims are clearly patentable over the recited references in view of the unexpected effect for transvaginal administration of 1, 25-dihydroxyvitamin D<sub>3</sub> for the treatment of hypocalcemia of domestic animals.

Withdrawal of all rejections and passage of the application to issue are therefore respectfully requested.

Respectfully submitted,



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